was washed with water, dried over Na_2SO_4, and evaporated under vacuum, and the residue was chromatographed on silica gel followed by purification by preparative TLC with hexane as the eluant to afford 146 mg (38%) of **12**: pale yellow prisms (MeOH); mp 181–183.5 °C; UV (cyclohexane) λ_{max} 216 nm (log ϵ 4.38), 230 (4.35, sh), 254 (4.28), 277 (4.04, sh), 336 (3.67); NMR ($CDCl_3$) δ 0.67, 1.14 (each 1 H, d, J = 8.5 Hz), 1.19, 1.33 (each 9 H, s), 1.88–2.50 (4 H, m), 2.17 (3 H, s), 3.02–3.34 (2 H, m), 6.17, 6.61 (each 1 H, d, J = 12.0 Hz), 6.24, 6.61 (each 1 H, s), 6.90, 6.97 (each 1 H, d, J = 1.7 Hz); ^{13}C NMR ($CDCl_3$) δ 149.06 (s), 147.48 (s), 141.49 (s), 138.79 (s), 137.79 (s), 137.50 (s), 135.09 (s), 133.98 (d), 133.63 (d), 132.45 (s), 130.28 (d), 126.70 (d), 126.35 (d), 121.82 (d), 65.29 (s), 40.57 (s), 36.22 (s), 34.87 (t), 34.11 (s), 32.06 (t), 31.41 (q), 30.18 (q), 29.19 (t), 26.24 (t), 18.44 (q); mass spectrum, m/e 488, 490, 492, 494 (M^+). Anal. Calcd for $C_{29}H_{35}Cl_3$: C, 71.09; H, 7.20. Found: C, 70.92; H, 7.25.

Reaction of 5b with Dichlorocarbene. To a stirred solution of 250 mg (0.667 mmol) of **5b** and 250 mg (0.900 mmol) of tetrabutylammonium chloride in 9 mL of chloroform and 12 mL of benzene was added with stirring 12 mL of 50% KOH aqueous solution at room temperature. After the solution was stirred vigorously for 24 h at room temperature, the reaction mixture was poured into a large amount of water. The organic layer was extracted with dichloromethane. The dichloromethane extract was washed, dried over Na_2SO_4, and evaporated under vacuum, and the residue was chromatographed on silica gel, followed by preparative TLC purification with hexane as the eluant to afford 162 mg (65%) of recovered **5b** and 46.5 mg (14%) of **14**: colorless crystals; mass spctrum, m/e 502, 504, 506, 508 (M^+).

X-ray Analysis of 7. Crystal data are as follows: $C_{30}H_{32}Cl_6$, M_r = 605.3, monoclinic; space group $P2_1/C$; a = 11.852 (5), b = 7.343 (1), and c = 18.459 (5) Å; β = 109.75 (2)°; V = 1512.0 Å^3; Z = 2; c = 1.33 g·cm^{-3}. The final R value is 0.133.

Acknowledgment. We thank Prof. G. K. Surya Prakash (Hydrocarbon Research Institute, University of Southern California) for revising our English usage for publication.

General Syntheses of 6- and 7-Carbomethoxy-*trans*-1-heteradecalins and 6- and 7-Carbomethoxy-*trans*-2-heteradecalins

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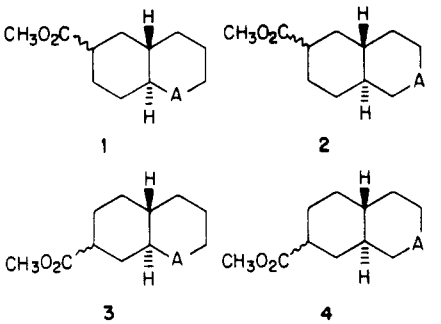
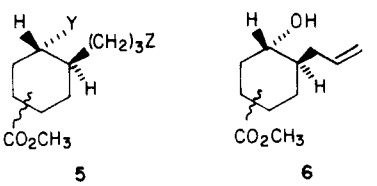
Two routes to all of the title compounds in the oxa and aza series have been studied. The most general path, involving a cyclohexene oxide intermediate, was not successful because of difficulty in separating regioisomers. Allylation of 4-carbomethoxycyclohexanone (**11**) followed by reduction produced the required trans-disubstituted allyl alcohols, which were converted to all of the desired 6-carbomethoxy-*trans*-1-heteradecalins. The allyl ketones were subjected to a homologation–side chain contraction sequence to produce the 6-carbomethoxy-*trans*-2-heteradecalins. Allylation of 3-carbomethoxycyclohexanone (**12**) was not regioselective, but all four product isomers were characterized. The desired 5-carbomethoxy-2-allylcyclohexanone isomers (**27** and **28**) were converted to the 7-carbomethoxy-*trans*-decalins by similar series of reactions.

Syntheses of *trans*-1- and -2-heteradecalin ring systems have been reported starting from acyclic, monocyclic, and bicyclic precursors.[1] When embarking on the syntheses of all of the 6- and 7-carbomethoxy-*trans*-1-heteradecalins and 6- and 7-carbomethoxy-*trans*-2-heteradecalins (**1–4**),[2] as we did several years ago in order to probe a variety of heteratom effects, the hope would be to develop a general synthetic route adaptable to all of the desired targets or, at least, a significant subset of targets. Our earlier attempts utilizing a variety of synthetic approaches[3-7] produced only isolated examples of the target systems, although a Robinson annulation route[5-8] promises to be general for all of the desired 2-heteradecalins.

For a general approach, retrosynthetic analysis suggests that the target compounds could all be obtained from a trans-disubstituted carbomethoxycyclohexane of type **5** provided that group Y could accommodate both a facile interchange between heteroatoms (to produce the 1-heteradecalins) and a homologation (to produce the 2-heteradecalins) and that group Z could be displaced by a variety



of heteroatoms and be easily shortened by one carbon. One such intermediate would be of type **6**, for which two approaches were deemed attractive.



If a 4-substituted cyclohexene formed signficant amounts of epimeric[2] epoxides **7** and **8**, the stereoelectronic requirement for trans-diaxial ring opening[9] of the epoxide by an allyl Grignard reagent, for example, would produce regioisomeric *trans*-2-allylcyclohexanols, one of which

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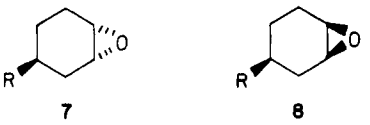
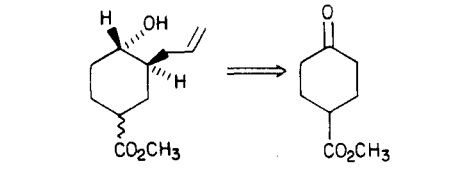


7 8

would lead to the target series **1** and **2** and the other of which would lead to series **3** and **4**. The feasibility of such ring opening–cyclization sequences has been shown for *trans*-1-oxadecalin[10] and, using an episulfide, for substituted *trans*-1-thiadecalins.[5,11] However, the inhereent difficulty in such a route is separation of the product mixtures and characterization of the regioisomers.

Alternatively, each regioisomer of type **6** (**9** and **10**) could be prepared separately from the appropriate cyclohexanones **11** and **12**. The problems here would be the need for regioselective introduction of the allyl group into ketone **12** and the need to establish the trans relationship of the allyl group and the hydroxyl function in both **9** and **10**.



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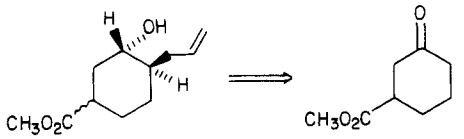
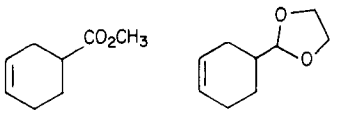


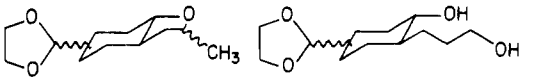
10 12

The Epoxide Route. The most obvious epoxidation substrate, 4-carbomethoxycyclohexene (**13**), was prepared from *p*-hydroxybenzoic acid by a sequence of hydrogenation over rhodium,[12] esterification, tosylation, and dehydrotosylation (using DBU in dioxane[13]). Epoxidation using MCPBA in CH_2Cl_2[14] gave a mixture of approximately 2:1 trans and cis epoxides[15,16] **7** and **8**, respectively (R = CO_2CH_3). Treatment of these epoxides with allyl Grignard reagent as such or in the presence of varying amounts of cuprous iodide[17,18] produced complex mixtures apparently containing significant quantities of products resulting from attack on the ester carbonyl. The feasibility of using lithium diallylcuprate[19] was not explored because of the availability[5] of large quantities of 4-(1,3-dioxolanyl)cyclohexene (**14**) and its epoxides.



13 14

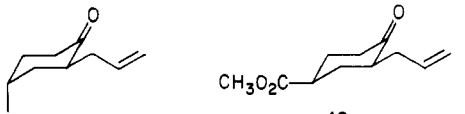
Epoxidation (MCPBA in CH_2Cl_2) produced a roughly 1:1 mixture of epoxides **7** and **8** (R = $\overline{CHOCH_2CH_2O}$). This epoxide mixture was treated with allylmagnesium chloride in THF at −20 °C in the presence of a catalytic amount of cuprous iodide[20] to produce the desired mixture of the two regioisomeric *trans*-allylcyclohexanols. This mixture was subjected to Lattes' oxymercuration–reduction procedure[10] which had produced the parent 1-oxadecalin. The oxymercuration reaction proved to be extremely sluggish under these conditions ($HgCl_2$), so mercuric acetate was utilized and the resulting organomercuric intermediate subjected to acetate–chloride exchange prior to reduction. Under all oxymercuration conditions attempted, the only products were five-membered cyclic ethers (**15**) resulting from Markovnikov regiochemistry.



15 16

The allylcyclohexanol mixture was then subjected to hydroboration–oxidation,[21] producing a mixture of diols **16**. Selective tosylation[22] of the primary alcohol followed by treatment with NaH in DMF[23] cleanly produced a 1:1 mixture of two *trans*-1-oxadecalins. The acetal proved stubborn to hydrolysis, but this could be accomplished over several days. Oxidation with Jones' reagent followed by diazomethane esterification produced a mixture of four carbomethoxy-*trans*-1-oxadecalins (**1** and **3**, A = O). Separation into a mixture of regioisomeric material with axial carbomethoxy groups and a mixture of regioisomeric material with equatorial carbomethoxy groups was accomplished with considerable effort, but further efforts to separate each regioisomeric pair at this point or at earlier stages of this synthesis failed or only produced small amounts of one pure regioisomer, a rather disappointing departure from the results[5] in the sulfur series.

The Ketone Route. A. The 6-Carbomethoxy-1-heteradecalins 1. The symmetrical substrate, 4-carbomethoxycyclohexanone (**11**), which would lead to the 6-carbomethoxy targets **1** and **2**, was studied first. The mixture of *cis*- and *trans*-4-carbomethoxycyclohexanol obtained en route to 4-carbomethoxycyclohexene (see above) was oxidized with PCC[24] to give ketone **11**. Allylation of the pyrrolidine enamine of **11** in refluxing dioxane produced a 50% yield after hydrolysis of a 4:1 mixture of stereoisomers **17** and **18**, respectively. These isomers were



17 18

separated and the structures were assigned based on spectral data. The major product is consistent with the tendency for preferred axial alkylation[25] of enamines.

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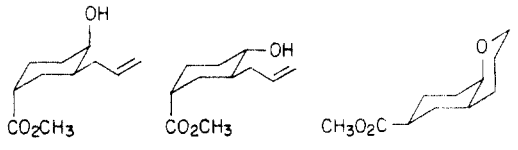
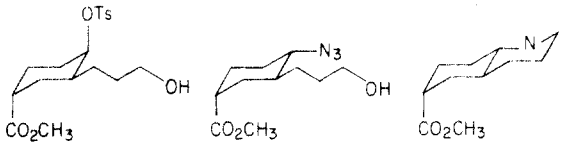
Treatment of ketone **11** with a Claisen rearrangement protocol[26,27] presumably involving an allyl enol ether produced a higher yield of a 1:1 mixture of **17** and **18**.

Sodium borohydride reduction of ketone **17** gave epimers **19** and **20**, which were separated and assigned structures based on spectral data. The trans epimer **20** was subjected to hydroboration–oxidation[21] followed by selective tosylation of the primary alcohol. This hydroxytosylate could not be efficiently cyclized in a variety of bases but could be cyclized to the axial epimer of 6-carbomethoxy-*trans*-1-oxadecalin (**1a**, A = O) by heating in HMPA at 80 °C. Ketone **18** was similarly treated to give the equatorial epimer of 6-carbomethoxy-*trans*-1-oxadecalin (**1e**, A = O) and the equatorial epimer of 6-carbomethoxy-*cis*-1-oxadecalin (**21**).



19 **20** **21**

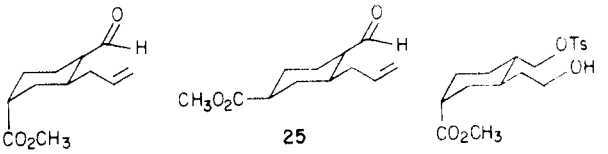
The route to the *trans*-1-azadecalin framework utilized the *cis*-allylcyclohexanol **19**. Tosylation was extremely sluggish because of steric hindrance but was accomplished in good yield. Hydroboration–oxidation produced hydroxytosylate **22**, which was treated with sodium azide to effect S_N2 displacement and realize the required trans relationship between the side chains to cyclize. A variety of one-step cyclization procedures failed,[1] so the azido alcohol **23** was converted to the tosylate and then reduced by catalytic hydrogenation to the aminotosylate, which cyclized spontaneously[28] to the axial 6-carbomethoxy-*trans*-1-azadecalin (**1a**, A = N).



22 **23** **1a** (A = N)

B. The 6-Carbomethoxy-2-heteradecalins 2. For the homologation–chain shortening sequence, ketone **17** was converted by a Wittig reaction to the methoxymethylene homologue.[29] When subjected to hydrolysis, the enol ether mixture was quite sluggish, producing a mixture of four isomeric aldehydes, suggesting that the ester group had epimerized under the reaction conditions. Treatment of the aldehyde mixture with sodium methoxide/methanol at reflux to equilibrate to the presumably more stable trans orientation of the relevant side chains reduced the number of isomers to three. Column chromatographic separation produced one pure aldehyde and a mixture of two other aldehydes. Structural assignments were not unambiguous based on spectral data, so the pure aldehyde and the mixture of aldehydes were carried through the subsequent steps in the hope of making comparisons with authentic samples of the 2-oxadecalins[6] derived from a different route.

The pure aldehyde was reduced to the corresponding alcohol with sodium borohydride, then converted to the tosylate, and subjected to ozonolysis with a dimethyl sulfide reductive workup.[30] The minor product was the desired tosylate aldehyde, while the major product was shown to be the intermediate ozonide by its spectral characteristics (δ 102 in the ^{13}C NMR spectrum) and by reduction of isolated material to the aldehyde on retreatment with dimethyl sulfide. The unusual stability of this ozonide to these standard reducing conditions is not readily explainable. However, it was utilized by substituting sodium borohydride reduction of the ozonide for the dimethyl sulfide treatment, leading directly to a hydroxytosylate **26**. Cyclization by heating in HMPA produced the axial epimer of 6-carbomethoxy-*trans*-2-oxadecalin (**2a**, A = O) which was identical with authentic material.[6] This also established that the pure aldehyde utilized had been structure **24**.



24 **25** **26**

Similar treatment of the mixture of two aldehydes produced a mixture of the equatorial epimer of 6-carbomethoxy-*trans*-2-oxadecalin (**2e**, A = O) (comparison with authentic sample[6]) and one isomer of 6-carbomethoxy-*cis*-2-oxadecalin, indicating that one of the components of the aldehyde mixture had been **25**.

With structure **24** unambiguously assigned to the pure aldehyde, the hydroxy tosylate in the above sequence (**26**) was treated with azide ion, converted to the tosylate, and subjected to catalytic hydrogenation, whereupon cyclization occurred to the axial epimer of 6-carbomethoxy-*trans*-2-azadecalin (**2a**, A = N).

C. The 7-Carbomethoxy-1-heteradecalins 3. The required starting material, 3-carbomethoxycyclohexanone (**12**), was prepared from *m*-hydroxybenzoic acid by using the same sequence as for its isomer **11**. Allylation of **12** was carried out by using the Claisen rearrangement[26,27] to give a mixture of four products. These four compounds were easily separable into two pairs chromatographically, but it was difficult to obtain more than small amounts of each compound in a pure state. Spectral data did not lead to unambiguous structural assignments, so each pair of isomers was deoxygenated by using sodium cyanoborohydride reduction[31] of the tosylhydrazones. This deoxygenation would introduce a plane of symmetry into the products derived from the desired 6-allyl ketones but not from the regioisomeric 2-allyl ketones. One product from each pair of ketones was methyl *trans*-4-allylcyclohexanecarboxylate, while the other product from each pair was a mixture of methyl 2-allylcyclohexanecarboxylates, indicating that each pair of ketones was a mixture of regioisomers and that equilibration had occurred during the deoxygenation, contrary to previous experience.[3]

In order to assign definitive structure to the ketones, the mixture of regioisomeric allylcyclohexanols obtained previously from epoxides **7** and **8** (R = $\overline{\text{CHOCH}_2\text{CH}_2\text{O}}$) was utilized. Hydrolysis of the acetal followed by Jones' oxidation and esterification with diazomethane furnished a mixture of esters, which could be separated sufficiently and characterized as regioisomers **18** and **27**. The equatorial

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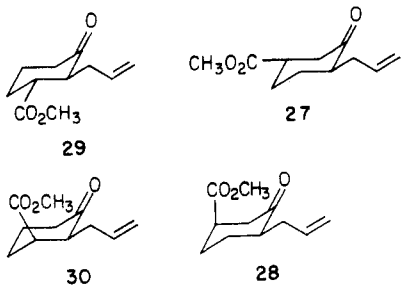
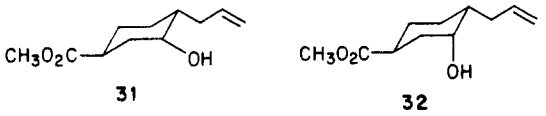
Chart I



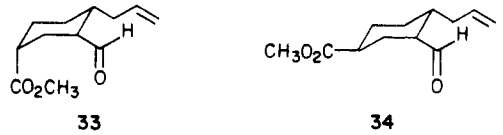
carbomethoxy groups in both compounds suggested that epimerization had occurred in this sequence. Structure **27** matched one of the allyl ketones obtained from the Claisen rearrangement. Equilibration of **27** with base permitted comparison with the epimeric ketone **28**. The allylation products were therefore assigned structures **29**, **27**, **30**, and **28** in terms of decreasing R_f values (Chart I), although the assignments to **29** and **30** remain tentative.

The mixture of **27** and **29** was reduced with sodium borohydride to yield four alcohols which were cleanly separable. The desired alcohols from **27**, **31**, and **32**, were assigned structures on the basis of spectral characteristics and retention times.



Alcohol **31** was treated as before (hydroboration–oxidation, monotosylation, cyclization) to give the equatorial epimer of 7-carbomethoxy-*trans*-1-oxadecalin (**3e**, A = O), which matched that reported previously.[3] Alcohol **32** was tosylated, subjected to hydroboration–oxidation, treated with sodium azide, tosylated, and reduced with cyclization to yield the equatorial epimer of 7-carbomethoxy-*trans*-1-azadecalin (**3e**, A = N).

D. The 7-Carbomethoxy-2-heteradecalins 4. Alcohol **32** was oxidized with PCC[24] to give ketone **27** in pure form. Homologation using the Wittig reaction[28] to introduce the methoxymethylene group as before followed by hydrolysis produced a mixture of four aldehydes. The two major isomers, which had the higher R_f values, were purified and tentatively assigned structures **33** and **34** based on spectral evidence. Aldehyde **33** was reduced to the alcohol, tosylated, subjected to reductive ozonolysis, and cyclized to produce the axial epimer of 7-carbomethoxy-*trans*-2-oxadecalin (**4a**, A = O), identical with an authentic sample.[6] Similarly, aldehyde **34** was converted to the corresponding equatorial epimer **4e** (A = O), identical with a previous sample.[6] These sequences confirmed the structures of both **33** and **34**.



The hydroxytosylate obtained from aldehyde **33** by the above sequence was treated with azide ion, tosylated, and cyclized on reduction to prepare the axial epimer of 7-carbomethoxy-*trans*-2-azadecalin (**4a**, A = N).

Conclusions

Synthetic procedures have been devised starting with the appropriate allylcarbomethoxycyclohexanones **17**, **18**, **27**, or **28** to prepare the target 6- and 7-carbomethoxy-substituted 1- and 2-oxa- and 1- and 2-azadecalins (**1–4**) by using general procedures. Each procedure could be modified to prepare the corresponding thiadecalins[5,7] by converting the appropriate hydroxytosylate to the ditosylate and cyclizing with sodium sulfide.[32]

The various azadecalin systems were somewhat unstable, so they were converted to the *N*-methyl derivatives by the method of Sondengam.[33]

Experimental Section

Melting points and boiling points are uncorrected. Infrared spectra were recorded on a Perkin-Elmer Model 567 grating infrared spectrophotometer. ^1H NMR spectra were obtained with either a Varian T-60 instrument or a JEOL-JNM FX270. Unless otherwise noted, all spectra were recorded by using $CDCl_3$ as solvent. Chemical shifts are reported in parts per million downfield from tetramethylsilane as the internal reference. ^{13}C NMR spectra were obtained with either a JEOL-JNM FX60Q or a JEOL-JNM FX270. All ^{13}C NMR spectra were recorded by using a complete decoupling program and, in certain cases, an INEPT program to assist in assignments of peaks. All reactions were routinely monitored by thin-layer chromatography using precoated silica gel glass plates (E. Merck). Spots were visualized under 254-nm UV light and/or by spraying with a solution of ceric sulfate, ammonium molybdate in 10% sulfuric acid, a 5% ethanolic phosphomolybdic acid solution solution, or a 10% solution of potassium permanganate in 1 N sodium hydroxide. On a routine basis, the products were purified by flash chromatography[34] on E. Merck 230–400 mesh silica gel. VPC analyses were performed on a Varian 5020 thermal conductivity GC instrument. The columns used were Carbowax 20M on Chromosorb W, SE-30, Carbowax 20M+ 2% KOH on Chromosorb W, and poly(phenyl ether) (five rings) on Anakron. Elemental analyses were performed by the Mikroanalytisches Laboratorium, Elbach, West Germany.

4-Hydroxycyclohexanecarboxylic Acid. A mixture of 1.0 g of *p*-hydroxybenzoic acid (70.2 mmol) and 140 mg of 5% Rh–Al_2O_3 in 10 mL of MeOH was shaken in a Parr bottle under 50 psi of hydrogen pressure[12] at 25 °C for 24 h, then filtered through a bed of Celite, and concentrated under reduced pressure to give 1.0 g of the desired product (97% yield) as a white solid (mixture of cis and trans isomers): mp 138–146 °C (lit.[35] mp 150 °C (cis), 120–121 °C (trans)): ^{13}C NMR δ 179.2, 70.5, 67.7, 42.1, 35.1, 32.7, 30.1, 28.3, 26.8, 26.4, 24.9.

4-Carbomethoxycyclohexanol. To a solution of 1.0 g of the 4-hydroxycyclohexanecarboxylic acids (6.94 mmol) in 10 mL of ether at 25 °C was slowly added a solution of diazomethane[36] in ether until the yellow color persisted. The excess diazomethane was purged with nitrogen, and the solution was concentrated to give 1 g of esterified product (91.1% yield) as an oil (mixture of cis and trans isomers): ^{13}C NMR δ 175.7, 69.3, 66.4, 51.2, 41.9, 41.0, 34.1, 31.7, 28.8, 26.9, 25.1, 23.5.

4-Carbomethoxycyclohexene (13). To a solution of 1.0 g of the above alcohol (6.3 mmol) in 5 mL of benzene were added 2.8 mL of pyridine and 1.3 g of *p*-toluenesulfonyl chloride[37] (6.9 mmol, 1.1 equiv). After being stirred at 25 °C for 24 h, the mixture was poured into 20 mL of H_2O and extracted with three 15-mL portions of ether. The combined ethereal extract was washed successively with 15 mL of 10% HCl, 15 mL of 2% $NaHCO_3$, and 10 mL of H_2O. The organic layer was dried ($MgSO_4$) and concentrated to give 2.0 g of tosylate as a yellow oil. This was used directly without purification.

A mixture of 2.0 g of tosylate (67.3 mmol) and 1.34 g of 1,8-diazabicyclo[5.4.0]undec-7-ene (DBU)[13] (8.8 mmol, 1.4 equiv) in 6 mL of dioxane was refluxed under a nitrogen atmosphere for 1 h. The cooled solution was diluted with 40 mL of ether and washed with 10 mL of 10% HCl, 10 mL of 5% $NaHCO_3$, and 10

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mL of H_2O, dried ($MgSO_4$), and concentrated to give 1.55 g of a crude oil. This oil was purified on a silica gel column, by eluting with 5% EtOAc/hexane to give 550 mg of cyclohexene **13** as a clear oil (62.3% yield): ^{13}C NMR δ 174.6, 126.5, 124.9, 51.5, 39.0, 27.1, 24.6, 24.2.

4-Carbomethoxycyclohexene Oxide (7 and 8, R = CO_2CH_3). To a solution of 1.0 g of cyclohexene **13** (7.1 mmol) in 10 mL of dry CH_2Cl_2 at 0 °C was added slowly a solution of 1.5 g of *m*-chloroperbenzoic acid (MCPBA)[14] (8.63 mmol, 12 equiv) in 5 mL of dry CH_2Cl_2. After being stirred at 0 °C for 2 h, the mixture was filtered. The filtrate was washed successively with 10 mL of saturated Na_2CO_3, 10 mL of saturated $NaHCO_3$, 10 mL of H_2O, and 10 mL of brine. The organic layer was dried ($MgSO_4$) and concentrated. Purification by vacuum distillation (bp 69–71 °C (0.25 mm)) yielded 700 mg (63% yield) of product, a clear oil, as a mixture of cis and trans isomers: ^{13}C NMR δ 174.9, 174.4, 51.4, 50.9, 50.5, 49.9, 37.1, 35.1, 26.6, 25.7, 23.4, 22.2, 20.5. Anal. Calcd for $C_8H_{12}O_3$: C, 61.52; H, 7.74; Found: C, 61.29; H, 7.74.

Attempts To Prepare 4-Carbomethoxy-2-allylcyclohexanols (9). To a slurry of 43 mg of cuprous iodide[20] (10 mol %) in 5 mL of dry THF at −20 °C under a nitrogen atmosphere was added dropwise 3.5 mL of a 1 M solution of allylmagnesium bromide in ether. After the mixture was stirred at −20 °C for 30 min, a solution of 350 mg of epoxides **7** and **8** (R = CO_2CH_3) (2.2 mmol) in 5 mL of dry THF was slowly added over a period of 10 min. The reaction was stirred at −20 °C for 1 h and at 0 °C for 30 min and then quenched by addition of 20 mL of a saturated solution of ammonium chloride. The layers were separated. The aqueous layer was extracted with three 10-mL portions of ether. The combined organic layer was washed with 10 mL of saturated $NaHCO_3$ and 10 mL of H_2O, then dried ($MgSO_4$), and concentrated to give 470 mg of a clear oil. The ^{13}C NMR spectrum of this oil exhibited three sets of resonances corresponding to olefinic carbons and one resonance at δ 85.5 corresponding to a tertiary alcohol carbon: ^{13}C NMR δ 134.4, 134.1, 133.4, 133.3, 118.2, 117.3, 85.5, 79.0, 78.0, 74.2, 71.9, 70.3, 68.2, 67.5, 52.2, 51.7, 43.4, 42.3, 40.8, 40.5, 39.0, 37.5, 30.1, 26.9, 26.2, 25.3, 24.1, 23.3, 17.9. A second attempt using 1 equiv of cuprous iodide gave similar results.

4-(1,3-Dioxolanyl)cyclohexene 1,2-Epoxides (7 and 8, R = $\overline{CHOCH_2CH_2O}$). Epoxidation of cyclohexene **14**[5] was performed following the above procedure. An isolated yield of 81.7% of a mixture of cis and trans isomers was obtained after vacuum distillation: bp 84–86 °C (0.35 mm); ^{13}C NMR δ 106.6, 54.7, 52.5, 52.1, 51.1, 50.8, 36.6, 33.7, 25.6, 24.3, 22.9, 21.2, 18.9.

4- and 5-(1,3-Dioxolanyl)-2-allylcyclohexanols. To 55 mg of purified cuprous iodide (10 mol %) in 5 mL of dry THF at −20 °C under a nitrogen atmosphere was added dropwise 4.6 mL of a 1 M solution of allylmagnesium bromide in ether[20] (4.6 mmol, 1 equiv). After the mixture was stirred at −20 °C for 10 min, a solution of 500 mg of epoxides **7** and **8** (R = $\overline{CHOCH_2CH_2O}$) (2.9 mmol) was added dropwise, and the reaction was allowed to warm to 0 °C over a period of 30 min. The reaction was worked up as in the previous case. The residue was diluted with ether and filtered through a bed of Florisil to give 160 mg (97.8% yield) of a clear oil, which was a mixture of two regioisomers: ^{13}C NMR δ 136.9, 136.7, 115.3, 106.2, 106.0, 70.6, 69.1, 64.4, 40.8, 39.2, 35.8, 35.5, 35.7, 30.8, 28.6, 26.8, 23.6, 22.2.

Oxymercuration–Demercuration of (1,3-Dioxolanyl)-2-allylcyclohexanols.[10] To 1.5 g of $Hg(OAc)_2$ (4.71 mmol, 1 equiv) in 4 mL of water was added 8 mL of THF. Deep yellow precipitates formed instantly. To this mixture was added dropwise a solution of 1.0 g of the allyl substrates (4.71 mmol) in 4 mL of THF. The yellow precipitates disappeared, and the solution turned colorless at the end of the addition. The mixture was stirred at 25 °C for 1 h, at which time the solution gave a negative test with 10% NaOH. The THF was removed at reduced pressure. The aqueous solution was extracted with three 10-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated. The residue was diluted with 30 mL of $CHCl_3$ and cooled at 0 °C, and a solution of 10% KCl was added dropwise. After the mixture was stirred at 25 °C for 18 h, the layers were separated. The aqueous layer was extracted with two 10-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated. The residue was dissolved in 12 mL of H_2O and 12 mL of 10% NaOH. The solution was cooled to 0 °C, and 150 mg of sodium borohydride in 2 mL of 10% NaOH was added dropwise. Black precipitates were formed instantly. The reaction was stirred at 0 °C for 1 h, and the aqueous layer was decanted and extracted with three 15-mL portions of ether. The combined ethereal layer was dried ($MgSO_4$) and concentrated to give 1.0 g of a crude oil, which was purified on a silica gel column. Elution with 20% EtOAc/hexane gave 620 mg of a clear oil (62% yield). The product was a mixture of two isomers (**15**): ^{13}C NMR δ 105.3, 104.8, 81.6, 77.3, 73.9, 64.3, 46.3, 41.2, 39.7, 39.3, 37.2, 36.5, 31.2, 29.0, 27.5, 25.5, 24.1, 21.9.

Diols 16. To a solution of 1.4 g of a mixture of (1,3-dioxolanyl)-2-allylcyclohexanols in 60 mL of dry THF at 0 °C was slowly added 6.6 mL of a 1 M solution of diborane in THF.[21] After the mixture was stirred at 0 °C for 1 h, 1.5 mL of water was added dropwise, and the stirring was continued for 15 min. The organoborane intermediate was oxidized by successive addition of 800 μL of 20% NaOH and 300 μL of a 30% H_2O_2 solution. The solution was then saturated with solid K_2CO_3, and the layers were separated. The aqueous layer was extracted with five 30-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated to give a crude oil. Chromatography on silica gel (elution with ethyl acetate) gave 800 mg of diols **16** as a clear oil (52.6% yield): ^{13}C NMR δ 106.3, 71.3, 69.7, 64.5, 62.1, 41.0, 39.2, 36.0, 35.7, 32.3, 31.2, 29.9, 27.4, 26.9, 25.3, 24.1, 22.5.

Monotosylation of Diols 16. To a solution of 900 mg of diols **16** (3.9 mmol) in 10 mL of pyridine at −20 °C was added 838 mg of *p*-toluenesulfonyl chloride[22] (4.3 mmol, 1.1 equiv). The mixture was kept at ca. −10 °C for 35 h and then diluted with 50 mL of ether. The ethereal solution was washed with three 10-mL portions of 1 N HCl and 10 mL of H_2O, then dried ($MgSO_4$), and concentrated. The residue was purified by chromatography (elution with 50% EtOAc/hexane), giving 510 mg of hydroxytosylates as a colorless oil (30.8% yield). TLC of this oil showed a very close double spot.

(1,3-Dioxolanyl)-*trans*-1-oxadecalins. To a slurry of 180 mg of prewashed sodium hydride (50% in mineral oil, 9.76 mmol, 1 equiv) in 2 mL of dry DMF was added at 25 °C a solution of 290 mg of the above hydroxytosylates (0.76 mmol) in 1 mL of DMF. The reaction was stirred at 25 °C for 20 h and then poured into 5 mL of ice–water. The aqueous solution was extracted with three 10-mL portions of ether. The combined ethereal extract was washed with 10 mL of H_2O, then dried ($MgSO_4$), and concentrated to give 110 mg of a crude oil. This oil was chromatographed (elution with 25% EtOAc/hexane) to give 90 mg of a colorless oil (55.6% yield). The purified oil was homogeneous on TLC; however, its ^{13}C NMR spectrum indicated a 1:1 mixture of two compounds: ^{13}C NMR δ 106.6, 81.6, 81.1, 68.2, 64.8, 41.8, 40.8, 40.6, 32.8, 32.0, 31.4, 30.5, 30.3, 26.6, 26.2, 25.3. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49; Found: C, 67.54; H, 9.24.

Carbomethoxy-*trans*-1-oxadecalins (1 and 3, A = O). A mixture of 200 mg of the above acetals (0.94 mmol) and 1 mL of 4 N HCl in 3 mL of THF was heated at 40–50 °C for 24 h. The mixture was cooled to 25 °C and neutralized by portionwise addition of solid $NaHCO_3$. The layers were separated, and the aqueous layer was extracted with five 30-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated to give 150 mg of aldehydes as an oil. This oil, which was homogeneous on TLC, was used directly in the next step.

To a solution of 150 mg of aldehydes in 10 mL of acetone at 0 °C was added dropwise a solution of Jones' reagent[38] until the reaction mixture remained orange. The reaction was then quenched by addition of isopropyl alcohol and diluted with 50 mL of CH_2Cl_2. Solid sodium acetate was added along with a large amount of $MgSO_4$. The mixture was stirred at 25 °C for 15 min and then filtered. The filtrate was concentrated to give 150 mg of an oil. This oil was used directly in the next step.

A solution of 150 mg of the above acids in 10 mL of ether at 25 °C was treated with an excess of an ethereal diazomethane[36] solution. The unreacted diazomethane was purged with a stream of N_2. The reaction was then concentrated under reduced pressure to yield 155 mg of an oil, which showed a very close double spot on TLC. The ^{13}C NMR spectrum of the products indicated a

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mixture of four isomers: ^{13}C NMR δ 175.6, 175.1, 174.9, and 174.4 (CO_2Me), 81.5, 81.2, 80.9, and 80.7 (C1), 42.5, 42.0, 38.2, and 37.8 (C6), 41.3, 40.8, 38.7, and 38.2 (C10).

Column chromatography (5% EtOAc/hexane) produced 30 mg of a mixture of two regioisomers: ^{13}C NMR δ 174.9 and 174.4 (CO_2Me), 81.5 and 81.2 (C1), 38.9 and 37.8 (C6), 38.7 and 38.2 (C10).

4-Carbomethoxycyclohexanone (11). A 50.0-g sample of *p*-hydroxybenzoic acid (0.36 mol) was hydrogenated as before. To the resulting methanolic solution of the saturated product was added 1 mL of concentrated H_2SO_4,[39] and the solution was heated at reflux for 20 h. The reaction was cooled to 25 °C, neutralized by addition of solid $NaHCO_3$, and then filtered. The filtrate was concentrated to give a yellow oil. This oil was dissolved in 300 mL of dry CH_2Cl_2. To this solution were added 100 g of Celite and, portionwise, 85 g of pyridinium chlorochromate[24] (PCC) (40 mmol, 1.2 equiv). After being stirred at 25 °C for 3 h, the mixture was filtered. The filtrate was concentrated under reduced pressure. The residue was diluted with 500 mL of ether and then filtered through a pad of Florisil. The filtrate was again concentrated. The residue was distilled under vacuum to yield 40.0 g of 4-carbomethoxycyclohexanone (11): bp 85–95 °C (1.2 mm) [lit.[40] bp 140 °C (20 mm)]; ^{13}C NMR δ 209 (C=O), 174.2 (CO_2Me), 51.6 (CO_2CH_3), 40.3 (C4), 39.4, 28.2.

Allylation of 4-Carbomethoxycyclohexanone (11). Method 1: Enamine Alkylation.[41] A mixture of 11.5 g of ketone **11** (73.7 mmol) and 8.5 g of pyrrolidine (138 mmol, 1.8 equiv) in 40 mL of benzene was refluxed with removal of water with a Dean–Stark trap. After 24 h, the intermediate enamine was isolated by distilling off solvents: yellow oil; IR 1735 (ester), 1640 cm^{-1} (C=C); ^{13}C NMR δ 176.0, 142.3, 90.7, 51.0, 47.1, 39.4, 26.4, 25.4, 24.3.

The enamine was dissolved in 40 mL of dioxane. To this solution at 25 °C was added dropwise 11.5 mL (120 mmol, 1.6 equiv) of allyl bromide, and the mixture was heated at reflux for 2 days and then cooled to 25 °C. To the cooled mixture was added 10 mL of H_2O, and the mixture was again heated at reflux for an additional 30 min. The cooled solution was extracted with three 20-mL portions of ether. The combined ether extract was washed with 30 mL of 1 N HCl and 20 mL of H_2O, then dried ($MgSO_4$), and concentrated. Chromatography (8% EtOAc/hexane eluent) gave 4.3 g of **17** (higher R_f), 1.9 g of **18** (lower R_f), and 3.9 g of recovered starting ketone. A combined yield of 42% was obtained.

17: oil; ^1H NMR δ 5.73 (m, 1 H), 5.04 (dd, J = 1.5 and 11.6 Hz, 1 H), 5.02 (d, J = 9.5 Hz, 1 H), 3.74 (s, 3 H), 2.85 (m, 1 H), 2.58–1.69 (9 H); ^{13}C NMR δ 210.6, 174.1, 135.3, 116.1, 51.5, 46.3, 38.2, 37.8, 33.4, 33.1, 28.1. Anal. Calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.21; Found: C, 67.42; H, 8.10.

18: oil; ^1H NMR δ 5.77 (m, 1 H), 5.03 (dd, J = 1.1 and 18 Hz, 1 H), 5.02 (d, J = 10 Hz, 1 H), 3.69 (s, 3 H), 2.81 (tt, J = 3.2 and 12.1 Hz, 1 H), 2.54–1.47 (9 H); ^{13}C NMR δ 209.7, 174.2, 135.7, 116.6, 51.7, 48.3, 41.9, 40.2, 34.9, 33.1, 29.5.

Method 2: Claisen Rearrangement.[26] A mixture of 10.0 g of ketone **11** (64.0 mmol), 8.0 g of allyl alcohol (141 mmol, 2.2 equiv), 7.35 g of 2,2-dimethoxypropane (70.5 mmol, 1.1 equiv), and 5 mg of *p*-toluenesulfonic acid monohydrate in 50 mL of benzene was distilled through a 6-in. distillation column. After ca. 25 mL of distillate (benzene, methanol, acetone) had been collected at 55–65 °C, the distillation was continued until the flask temperature reached 190 °C, at which time the head temperature was 90 °C. Distillation of the clear, yellow liquid was then continued at reduced pressure to give 11.0 g of a clear oil [bp 90–100 °C (0.15 mm)]. A combined yield of 73% was obtained. The TLC of this oil showed a mixture of two compounds with the same R_f's as **17** and **18** (above). Chromatography (elution with 2 L of 7% EtOAc/hexane and 1 L of 20% EtOAc/hexane) gave 3.2 g of **17**, 3.1 g of **18**, and 4.5 g of a 1:1 mixture of them. Spectral data of these compounds were identical with those of the previously prepared products.

4-Carbomethoxy-2-allylcyclohexanols (19 and 20). To a solution of 500 mg of ketone **17** (2.55 mmol) in 3 mL of methanol at 0 °C was added slowly 97 mg of sodium borohydride[42] (2.55 mmol, 4 equiv). After being stirred at 0 °C for 15 min, the mixture was poured into 15 mL of a saturated ammonium chloride solution. The aqueous solution was then extracted with three 10-mL portions of ether. The combined ethereal extract was washed with 20 mL of H_2O, then dried ($MgSO_4$), and concentrated to give 498 mg of a crude oil. TLC showed two close spots. This mixture was separated by chromatography (elution with 10% EtOAc/hexane) to give 257 mg of **19** (cis isomer, higher R_f) and 165 mg of **20** (trans isomer, lower R_f). An isolated yield of 83.5% was obtained.

19 (cis isomer): oil; ^1H NMR δ 3.8 (br s, 1 H, C*H*OH); ^{13}C NMR δ 175.8, 137.0, 115.9, 69.1 (C1), 51.4, 37.9 (C2 and C4), 33.9, 29.4, 28.1, 23.1.

20 (trans isomer): oil; ^1H NMR δ 3.3 (dt, 1 H, C*H*OH); ^{13}C NMR δ 175.8, 136.7, 116.2, 72.6 (C1), 51.5, 40.6 (C2), 38.4 (C4), 36.6, 30.9, 30.1, 25.0.

4-Carbomethoxy-2-(3-hydroxypropyl)cyclohexanol. To a solution of 850 mg of 2-allylcyclohexanol **20** (4.3 mmol) in 10 mL of dry THF at 0 °C under a nitrogen atmosphere was added slowly a 1 M solution of diborane[21] in THF. After the mixture was stirred at 0 °C for 1 h, 2 mL of H_2O was slowly added, and the stirring was continued for an additional 30 min at 0 °C. The organoborane intermediate was subsequently oxidized by successive addition of 1 mL of 20% NaOH and 400 μL of 30% H_2O_2 solution. The mixture was then saturated with solid K_2CO_3, and the layers were separated. The aqueous layer was extracted with five 10-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated to give a crude oil. Chromatographic purification (EtOAc as eluant) gave 510 mg (55% yield) of diol as a colorless oil.

The Axial Epimer of 6-Carbomethoxy-*trans*-1-oxadecalin (1a, *A* = O). To a solution of 450 mg of the above diol (2.08 mmol) at −30 °C in 2 mL of pyridine was added 396 mg of *p*-toluenesulfonyl chloride[22] (2.08 mmol, 1 equiv). After being stirred at −30 °C for 30 min, the reaction was maintained at −10 °C for 20 h and then diluted with 30 mL of ether. The ethereal solution was washed with three 10-mL portions of a saturated cupric sulfate solution and 10 mL of H_2O, then dried ($MgSO_4$), and concentrated to give 580 mg of a crude oil. TLC showed a small amount of a side product. This oil, however, was used directly in the next reaction.

The crude hydroxytosylate (580 mg) in 3 mL of hexamethylphosphoramide (HMPA) was heated at 75 °C for 2.5 h. The cooled mixture was diluted with 10 mL of ether and washed with two 5-mL portions of H_2O. The organic layer was dried ($MgSO_4$) and concentrated to give 375 mg of a crude oil. This oil was chromatographed (elution with 8% EtOAc/hexane) to give 181 mg (44% yield from diol) of a colorless oil. This oil solidified upon storage at −10 °C. TLC of the product showed one single spot; however, GC (Carbowax 20 M, 160 °C) exhibited two peaks at t_r 18.4 min (major peak) and t_r 20.2 min (minor, about 5%). Spectral data indicated the major component to be the desired compound with an axial carbomethoxy group:[3] ^1H NMR δ 3.94 (d of m, 1 H, H equatorial), 3.68 (s, 3 H, axial CO_2CH_3), 3.64 (s, 0.2 H, equatorial CO_2CH), 3.42 (dt, J = 2.7 and 11.6 Hz, 1 H, H9), 2.88 (dt, J = 4.2 and 10 Hz, 1 H, H2 axial), 2.63 (br s, 1 H, H6 equatorial), 2.26–1.07 (11 H) (lit.[3] δ 4.00, 3.72, 3.41, 2.93); ^{13}C NMR δ 174.9 (CO_2Me), 81.5 (C9), 68.3 (C2), 51.4 (CO_2CH_3), 38.9 (C10), 38.2 (C6), 32.5 (C5), 30.4 (C4), 29.0 (C8), 26.5 (C3), 25.8 (C7). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.60; H, 9.08.

The Equatorial Epimer of 6-Carbomethoxy-*trans*-1-oxadecalin (1e, A = O). This compound was prepared by following the same procedures used for the preparation of the axial epimer starting from the 4-carbomethoxy-2-allylcyclohexanone 18: ^1H NMR δ 3.94 (d of m, 1 H, H2 equatorial), 3.64 (s, 3 H, equatorial CO_2Me), 3.42 (dt, 1 H, H9), 2.9 (m, 1 H, H2 axial), 2.35 (tt, 1 H, H6 axial); ^{13}C NMR δ 175.6 (CO_2Me), 81.0 (C9), 68.4 (C2), 51.5 (CO_2CH_3), 42.6 (C6), 40.9 (C10), 34.1 (C5), 31.5 (C4), 30.3 (C8), 27.5 (C3), 26.6 (C7). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.88; H, 9.27.

The Equatorial Epimer of 6-Carbomethoxy-*cis*-1-oxadecalin (21). This compound was prepared following the same

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reaction sequence used for the preparation of **1a** (A = O) starting from ketone **18**. The 4(e)-carbomethoxy-*cis*-2-allylcyclohexanol resulting from the sodium borohydride reduction of **18** was used for the subsequent steps: ^{13}C NMR δ 174.9 (CO_2Me), 74.1 (C9), 68.9 (C2), 51.4 (CO_2CH_3), 43.1 (C6), 34.6 (C10), 31.4 (C5), 29.0 (C4), 27.8 (C8), 23.0 (C3), 21.0 (C7). Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.40; H, 9.06.

Tosylation of *cis*-2-Allylcyclohexanol 19. To a solution of 246 mg of *cis*-2-allylcyclohexanol **19** (1.24 mmol) in 2 mL of pyridine was added 472.3 mg of *p*-toluenesulfonyl chloride[37] (2.4 mmol, 2 equiv). After being stirred at 25 °C for 5 days, the reaction mixture was diluted with 20 mL of ether and washed with three 5-mL portions of a saturated $CuSO_4$ solution and then with 5 mL of water. The organic layer was dried ($MgSO_4$) and concentrated. The residue was purified chromatographically (10% EtOAc/hexane) to give 279 mg of the tosylate (64% yield): clear oil; ^{1}H NMR δ 7.8 (d, 2 H, Ar), 7.3 (d, 2 H, Ar), 5.6 (m, 1 H), 4.95 (m, 2 H), 4.7 (br s, 1 H), 3.63 (s, 3 H), 2.63 (m, 1 H), 2.45 (s, 3 H), 2.15–1.18 (12 H); ^{13}C NMR δ 175.0, 144.4, 135.4, 134.4, 129.6, 127.4, 116.5, 81.5, 51.4, 37.4, 36.9, 34.3, 27.6, 27.1, 21.4.

Hydroxytosylate 22. To a solution of 192 mg of the above tosylate in 3 mL of dry THF at 0 °C under a nitrogen atmosphere was added dropwise 1 mL of a 1 M diborane solution in THF (1 mmol, 1.85 equiv). After the mixture was stirred at 0 °C for 1 h, 560 μL of H_2O was slowly added. The stirring was continued for an additional 15 min, and then 330 μL of 20% NaOH was added along with 112 μL of 30% H_2O_2. The reaction was stirred at 0 °C for 30 min and then worked up as before. The resulting crude product was purified chromatographically (50% EtOAc/hexane), giving 85 mg of hydroxytosylate **22** as an oil (42.5% yield): ^{13}C NMR δ 175.2, 129.7, 127.6, 81.6, 62.5, 51.5, 37.7, 37.0, 29.7, 28.2, 27.3, 26.4, 25.4, 21.5.

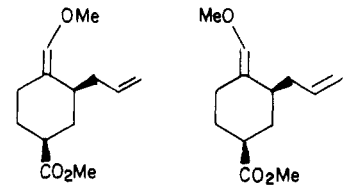
Azido Alcohol 23. A mixture of 45 mg of hydroxytosylate **22** (0.12 mmol) and 40 mg of sodium azide[43] (0.6 mmol, 5 equiv) in 1 mL of DMF was heated at 80 °C for 2 h. The cooled mixture was poured into 5 mL of water and then extracted with three 5-mL portions of ether. The combined ethereal extract was washed with 5 mL of water, then dried ($MgSO_4$) and concentrated to give 25 mg of azido alcohol **23** as a clear oil (80.7% yield). This product was clean on TLC and was used without purification: IR 3400 (OH), 2108 (N_3), 1730 cm^{-1} (CO_2Me); ^{13}C NMR δ 175.3, 63.6, 62.7, 51.6, 38.0, 30.1, 29.6, 28.3, 27.0, 25.0.

Tosylation of Azido Alcohol 23. To a solution of 100 mg of azido alcohol **23** (0.41 mmol) in 2 mL of pyridine at 25 °C was added 120 mg of *p*-toluenesulfonyl chloride (0.6 mmol, 1.5 equiv). After being stirred at 25 °C for 2 h, the mixture was diluted with 20 mL of ether, washed with three 5-mL portions of saturated $CuSO_4$ and then with 5 mL of H_2O. The organic layer was dried ($MgSO_4$) and concentrated. The residue was chromatographed (20% EtOAc/hexane) to give 136 mg of azidotosylate as a yellow oil (77.8% yield): IR 2090 (azide), 1735 cm^{-1} (ester); ^{1}H NMR δ 7.78 (d, 2 H), 7.33 (d, 2 H), 4.02 (dt, 2 H), 3.66 (s, 3 H), 3.05 (dt, 1 H), 2.58 (m, 1 H), 2.44 (s, 3 H), 2.44–1.19 (13 H); ^{13}C NMR δ 174.6, 144.6, 129.7, 127.7, 70.3, 63.4, 51.6, 37.9, 37.7, 30.1, 28.0, 27.0, 26.0, 25.0, 21.5. Anal. Calcd for $C_{18}H_{25}O_5N_3S$: C, 54.66; H, 6.37; N, 10.62; S, 8.10. Found: C, 54.74; H, 6.34; N, 10.48; S, 8.01.

The Axial Epimer of 6-Carbomethoxy-*trans*-2-azadecalin (1a, A = N). A mixture of 420 mg of the above azidotosylate (1.06 mmol) and 42 mg of 10% Pd/C in 5 mL of methanol was shaken in a Parr bottle under 30 psi of hydrogen pressure at 25 °C for 3 h.[44] The mixture was filtered through a bed of Celite and then concentrated to give 340 mg of the desired product as a white wax (86.6% yield): ^{13}C NMR (CD_3OD) δ 175.0, 129.7, 126.9, 61.2, 45.9, 39.5, 36.9, 33.5, 30.3, 27.6, 26.5, 23.6, 21.2.

This crude material (340 mg) was taken up in 10 mL of saturated $NaHCO_3$ and extracted with five 10-mL portions of CH_2Cl_2. The organic layer was washed with 10 mL of H_2O, then dried ($MgSO_4$), and concentrated to give 166 mg of the axial epimer of 6-carbomethoxy-*trans*-1-azadecalin (**1a**, A = N) as an oil (90.9% yield): IR 3330, 1735 cm^{-1}; ^{1}H NMR δ 3.64 (s, 3 H, CO_2CH_3), 3.02 (dm, J = 12, 1 H, H2 equatorial), 2.64 (br s, 1 H, H6 equatorial), 2.61 (dt, J = 3 and 12 Hz, 1 H, H2 axial), 2.20–0.95 (13 H); ^{13}C NMR δ 175.2 (CO_2CH_3), 61.5 (C9), 51.4 (CO_2CH_3), 47.0 (C2), 39.3 (C6, C10), 33.2 (C5), 32.0 (C4), 30.2 (C8), 27.0 (C3), 26.3 (C7). Anal. Calcd for $C_{11}H_{19}NO_2 \cdot 0.35H_2O$: C, 64.89; H, 9.75; N, 6.88. Found: C, 65.25; H, 9.44; N, 6.34.

Preparation of Enol Ethers 35. To a slurry of 11.2 g of methoxymethylphosphonium chloride[29] (32.7 mmol, 1.5 equiv) in 80 mL of dry THF at 0 °C under a nitrogen atmosphere was added slowly 22 mL of a 1.43 M solution of potassium *tert*-amylate (12.7 mmol, 1.5 equiv) in toluene. The resulting red ylide solution was stirred for 1 h at 0 °C. To this ylide solution at 0 °C was slowly added a solution of 4.3 g of ketone **17** (21.9 mmol) in 20 mL of THF. The red color faded upon addition of the ketone solution. After being stirred for 1 h at 0 °C and 3 h at 25 °C, the reaction was quenched by addition of glacial acetic acid and then poured into 500 mL of brine. The aqueous layer was then extracted with three 200 mL portions of ether. The combined ethereal extract was washed with 100 mL H_2O, then dried ($MgSO_4$), and concentrated. The residue was chromatographed (5% EtOAc/hexane), giving 2.8 g of enol ethers **35** as a clear oil (60% yield). This product was homogeneous on TLC. However, its ^{13}C NMR spectrum was consistent with the presence of *E* and *Z* isomers: ^{13}C NMR δ 140.3, 139.3, 137.1, 137.0, 133.5, 128.6, 128.4, 116.1, 115.6, 59.3, 51.4, 43.4, 38.5, 37.6, 36.8, 36.2, 35.9, 34.0, 35.5, 31.8, 30.4, 29.5, 29.2, 24.7, 20.4.



(*Z*)-**35** (*E*)-**35**

Hydrolysis of Enol Ethers 35. To a solution of 2.7 g of enol ethers **35** (12.0 mmol) in 40 mL of THF was added 10 mL of a 2 N HCl solution. After being stirred at 25 °C for 24 h, the reaction was neutralized by addition of solid $NaHCO_3$. The layers were separated. The aqueous layer was extracted with five 30-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated to give 2.2 g of an oil (87.3% yield). TLC showed a double spot, but the NMR spectral data suggested a mixture of four isomers (^{1}H NMR showed four resonances for aldehydic protons and ^{13}C NMR showed four sets of resonances): ^{1}H NMR δ 9.85 (s), 9.71 (s), 9.60 (d, J = 1.6 Hz), 9.59 (d, J = 3.7 Hz); ^{13}C NMR δ 204.3, 203.9, 175.7, 175.3, 175.1, 136.1, 136.0, 135.6, 135.0, 117.4, 117.0, 116.9, 116.8, 54.1, 52.2, 51.9, 51.5, 48.7, 43.1, 42.4, 38.5, 37.9, 37.8, 37.6, 37.4, 36.2, 33.3, 33.1, 32.9, 32.1, 31.3, 30.9, 30.5, 27.3, 26.7, 25.5, 24.9, 21.4, 20.

Epimerization and Isolation of Aldehydes from 35. A mixture of 2.2 g of the aldehyde mixture and 220 mg of sodium methoxide in 50 mL of methanol was refluxed under a nitrogen atmosphere for 2 days. The cooled mixture was poured into 200 mL of saturated NH_4Cl and extracted with four 50-mL portions of ether. The combined ethereal extract was washed with 50 mL of water, then dried ($MgSO_4$), and concentrated to give 2.1 g of a crude oil. The ^{13}C NMR spectrum of this oil exhibited three sets of resonances corresponding to three aldehydes: ^{13}C NMR δ 204.3, 203.9, 136.0, 135.5, 135.0, 117.4, 117.0, 116.9, 54.0, 52.1, 51.9, 51.5, 50.5, 48.7, 42.3, 38.5, 37.9, 37.6, 37.4, 36.2, 33.3, 33.0, 32.8, 32.1, 30.8, 30.4, 27.2, 26.7, 25.5, 21.3, 20.1.

The above mixture was chromatographed (elution with 3 L of 10% EtOAc/hexane and 500 mL of 40% EtOAc/hexane). Three fractions were obtained: fraction 1 (760 mg) of aldehyde A (later shown to be **24**); fraction 2 (560 mg) of a mixture of the three aldehydes; fraction 3 (830 mg) of aldehydes B and C (one of which was later shown to be **25**).

Aldehyde A (**24**): oil; ^{1}H NMR δ 9.60, (d, J = 1.6 Hz, aldehyde H), 5.75 (m, 1 H), 5.04 (m, 2 H), 3.67 (s, 3 H), 2.62 (m, 1 H), 2.4–1.4 (11 H); ^{13}C NMR δ 204.3, 175.1, 135.6, 117.0, 52.2, 51.5, 38.0, 37.6, 32.1, 30.5, 25.5, 21.4.

Aldehydes B and C: oil; ^{1}H NMR δ 9.7 (d, J = 3.7 Hz), 5.75 (m, 1 H), 5.03 (m, 2 H), 3.65 (s, 3 H), 2.6–1.1 (11 H); ^{13}C NMR δ 204.1, 136.0, 135.0, 117.5, 117.0, 54.1, 52.0, 51.6, 42.4, 38.6, 37.5, 36.2, 33.4, 33.1, 32.9, 30.9, 27.3, 26.8, 25.6, 20.2.

(43) Cleophax, J.; Anglesio, D.; Gero, S. D.; Guthrie, R. D. *Tetrahedron Lett.* **1973**, 1769.

(44) Sztaricskai, F.; Pelyvas, I.; Bognar, R.; Tamas, J. *Acta Chim. Hung.* **1983**, *112*, 275.

Reduction and Tosylation of Aldehyde A (24). To a solution of 280 mg of aldehyde A (24) (1.3 mmol) in 2 mL of MeOH at 0 °C was added 50 mg of sodium borohydride (1.3 mmol, 4 equiv). After being stirred at 0 °C for 15 min, the reaction mixture was poured into 30 mL of a saturated NH_4Cl solution and then extracted with three 20 mL portions of ether. The combined ethereal extract was washed with 20 mL of H_2O, then dried ($MgSO_4$), and concentrated to give 272 mg of alcohol (96% yield) as a clear oil. This product was essentially clean (TLC) and was used without purification.

This alcohol was converted to the tosylate by using the above procedure. Chromatography (15% EtOAc/hexane) yielded product as a clear oil (92.4% yield): ^{13}C NMR δ 175.7, 144.5, 136.2, 130.0, 129.6, 127.5, 116.0, 71.6, 51.2, 38.6, 36.8, 33.1, 30.4, 27.1, 22.5, 21.2. Anal. Calcd for $C_{19}H_{26}O_5S$: C, 62.27; H, 7.15; S, 8.27. Found: C, 62.29; H, 7.12; S, 8.68.

Ozonolysis to the Tosyl Aldehyde. Through a solution of 275 mg of the above unsaturated tosylate (0.76 mmol) in 30 mL of CH_2Cl_2 at −78 °C was bubbled a stream of ozone[45] until the solution turned deep blue. The excess ozone was then purged with a stream of air. Excess dimethyl sulfide[30] was added, and the mixture was stirred at 25 °C for 24 h. TLC of the reaction mixture showed two spots. The solvents were removed, and the residue was chromatographed (25% EtOAc/hexane). The first fraction (147 mg) was characterized as the ozonide: oil; ^{13}C NMR δ 173, 144, 132, 129.7, 127.7, 102.9, 93.7, 71.8, 51.5, 38.9, 37.3, 31.5, 29.7, 28.1, 27.1, 22.7, 21.5. The second fraction (60 mg) was the desired tosyl aldehyde: oil; ^{13}C NMR δ 201.1, 144.8, 129.4, 127.8, 72.0, 51.6, 47.3, 39.8, 38.5, 31.9, 29.7, 25.6, 24.8, 21.5.

Reduction of Ozonide. In an effort to confirm the structure of the ozonide, 147 mg of the ozonide was dissolved in 10 mL of CH_2Cl_2, and a large excess of dimethyl sulfide[30] was added. After the mixture was stirred at 25 °C for 2 days, TLC showed disappearance of ozonide and appearance of tosylaldehyde. The solvents were removed. The residue was diluted with 20 mL of ether and washed with two 5-mL portions of water. The organic layer was dried ($MgSO_4$) and concentrated to give 121 mg of a yellow oil with spectral characteristics identical with those of the tosyl aldehyde (above).

Ozonolysis and Reduction to the Tosyl Alcohol 26. To a solution of 1.2 g of the unsaturated tosylate from aldehyde A (3.35 mmole) in 30 mL of MeOH at −78 °C was bubbled a stream of ozone until the solution turned deep blue (ca. 30 min). The excess ozone was then removed by air, resulting in a clear, colorless solution. This solution was warmed to 0 °C, and 400 mg of sodium borohydride (10.5 mmol, 3.1 equiv) was added. After being stirred at 0 °C for 1 h, the solution was poured into 200 mL of saturated NH_4Cl and extracted with four 50-mL portions of ether. The combined ethereal extract was washed with 30 mL of water, then dried ($MgSO_4$), and concentrated. The residue was chromatographed (66% EtOAc/hexane), giving 1.1 g of the desired alcohol as a clear oil (90% yield): ^1H NMR δ 7.76 (d, 2 H), 7.32 (d, 2 H), 4.05 (dd, 1 H), 3.92 (dd, 1 H), 3.63 (s, 3 H), 2.57 (m, 1 H), 2.43 (s, 3 H), 2.11–1.23 (13 H); ^{13}C NMR δ 175.3, 144.7, 132.7, 129.7, 127.8, 72.3, 60.2, 51.5, 39.4, 38.4, 35.3, 31.1, 30.6, 25.3, 24.4, 21.5. Anal. Calcd for $C_{18}H_{26}O_6S$: C, 58.36; H, 7.07; S, 8.65. Found: C, 58.22; H, 7.04; S, 8.49.

The Axial Epimer of 6-Carbomethoxy-*trans*-2-oxadecalin (2a, A = O). A mixture of 100 mg of the above hydroxy tosylate **26** (0.27 mmol) in 2 mL of hexamethylphosphoramide[46] was heated at 70–80 °C for 2 h. The cooled mixture was diluted with 20 mL of ether and washed with two 5-mL portions of water, then dried ($MgSO_4$), and concentrated to give 39 mg of an essentially pure product (TLC) as an oil (75% yield): ^{13}C NMR δ 175.3 (CO_2Me), 72.8 (C1), 68.4 (C3), 51.4 (CO_2CH_3), 42.2 (C9), 39.2 (C6), 37.0 (C10), 33.5 (C4), 33.2 (C5), 26.7 (C8), 24.3 (C7).

The Equatorial Epimer of 6-Carbomethoxy-*trans*-2-oxadecalin (2e, A = O) and a Cis Isomer. A mixture of 6-carbomethoxy-2-oxadecalins was prepared following the same procedures used for the preparation of the axial epimer **2a** (A = O) starting from the mixture of aldehydes B and C. All of the intermediate pairs as well as the final product mixture were not separable. The ^{13}C NMR spectrum of this mixture exhibited two sets of resonances, one of which belonged to **2e** (A = O):[6] ^{13}C NMR δ 175.7 (CO_2Me), 72.7 (C1), 68.4 (C3), 51.5 (CO_2CH_3), 43.1 (C6), 41.7 (C9), 40.2 (C10), 35.0, 33.0, 28.2, 27.0 (lit.[6] identical). The other set of resonances corresponded to a cis-fused isomer: ^{13}C NMR δ 175.7 (CO_2Me), 72.7 (C1), 68.4 (C3), 51.5 (CO_2CH_3), 37.7 (C6), 35.9 (C9), 34.0 (C10), 32.7, 28.7, 26.3, 23.9.

Azido Alcohol from 26. To a solution of 1.1 g of hydroxytosylate **26** (2.76 mmol) in 10 mL of DMF was added 950 mg of sodium azide[43] (13.8 mmol, 5 equiv). The mixture was heated at 85 °C for 3 h, then cooled to 25 °C, and poured into 20 mL of water. The aqueous solution was extracted with three 30-mL portions of ether. The combined ethereal extract was washed with 20 mL of water, dried ($MgSO_4$), and concentrated to give 626 mg of azido alcohol as an oil (85% yield): ^1H NMR δ 3.68 (m, 2 H), 3.66 (s, 3 H), 3.44 (dd, J = 6.8 and 12 Hz, 1 H), 3.26 (dd, J = 7 and 12 Hz, 1 H), 2.61 (m, 1 H), 1.9–1.16 (11 H); ^{13}C NMR δ 175.5, 60.4, 54.6, 51.6, 40.0, 38.6, 35.5, 32.1, 30.7, 25.5. This oil was clean by TLC and was used directly in the next step without further purification.

Azido Tosylate. To a solution of 600 mg of the above azido alcohol (2.49 mmol) in 5 mL of pyridine at 25 °C was added 600 mg of *p*-toluenesulfonyl chloride (31.5 mmol, 1.2 equiv).[44] After being stirred at 25 °C for 3 h, the reaction mixture was worked up as before. The residue was chromatographed (20% EtOAc/hexane) to give 660 mg of azido tosylate as an oil (67%): ^1H NMR δ 7.79 (d, J = 7.9 Hz, 2 H), 7.34 (d, J = 7.3 Hz, 2 H), 4.05 (m, 1 H), 3.66 (s, 3 H), 3.31 (dd, J = 4.7 and 12 Hz, 1 H), 3.19 (dd, J = 6.5 and 12 Hz, 1 H), 2.56 (m, 1 H), 2.44 (s, 3 H), 2.11–0.85 (11 H); ^{13}C NMR δ 175.0, 144.7, 133.0, 129.8, 127.8, 68.2, 54.4, 51.6, 39.7, 38.4, 32.0, 31.9, 30.4, 25.3, 21.5. Anal. Calcd for $C_{18}H_{25}N_3O_5S$: C, 54.66; H, 6.37; N, 10.62; S, 8.17. Found: C, 54.74; H, 6.35; N, 10.49; S, 8.17.

The Axial Epimer of 6-Carbomethoxy-*trans*-2-azadecalin (2a, A = N). A mixture of 590 mg of the above azido tosylate (1.49 mmol) and 60 mg of 10% Pd/C in 10 mL of methanol was shaken in a Parr bottle under 30 psi of hydrogen pressure at 25 °C for 1.5 h. The reaction mixture was then filtered through a bed of Celite. The filtrate was concentrated to yield 530 mg of a white wax. This wax was taken up in 20 mL of a saturated $NaHCO_3$ solution and then extracted with five 20-mL of CH_2Cl_2. The combined organic layer was washed with 20 mL of brine, then dried ($MgSO_4$), and concentrated to give 173 mg of the desired **2a** (A = N) as a white solid (58.9% yield): ^1H NMR δ 3.65 (s, 3 H), 3.06 (d of m, 1 H), 2.88 (d of m, 1 H), 2.78 (br s, 1 H), 2.69 (br s, 1 H), 2.62 (m, 1 H), 2.23 (m, 1 H), 2.19 (m, 1 H), 2.0 (m, 1 H), 1.52–1.17 (8 H); ^{13}C NMR δ 175.5 (CO_2Me), 52.3 (C1), 51.4 (CO_2CH_3), 46.7 (C3), 42.8 (C9), 39.3 (C10), 37.9 (C6), 33.9 (C4), 33.4 (C5), 26.9 (C8), 26.6 (C7). Anal. Calcd for $C_{11}H_{19}NO_2 \cdot 0.35H_2O$: C, 64.89; H, 9.75; N, 6.88. Found: C, 65.23; H, 9.24; N, 6.37.

3-Carbomethoxycyclohexanone (12). This compound was prepared by starting from *m*-hydroxybenzoic acid following the same sequence used for the preparation of 4-carbomethoxycyclohexanone (11). The product was isolated in 70% yield in three steps: bp 75–90 °C (1.0 mm) [lit.[47] bp 115–120 °C (20 mm)]; ^{13}C NMR δ 208.5, 173.7, 51.6, 42.7, 40.5, 27.3, 24.0.

Allylation of 3-Carbomethoxycyclohexanone (12). A mixture of 17.0 g of ketone **12** (0.11 mol), 24.0 mL of allyl alcohol (0.36 mol, 3.3 equiv), 21.5 mL of 2,2-dimethoxypropane (0.72 mol, 6.6 equiv), and 7 mg of *p*-toluenesulfonic acid in 120 mL of benzene[26] was distilled through a 6-in. distillation head. When all the low boiling materials had been removed, the distillation was continued under reduced pressure, resulting in the isolation of 21.0 g of a mixture of products [bp 90–95 °C (0.15 mm)] as a clear oil (97.4% combined yield).

The product mixture was chromatographed (elution with 1 L of 15% EtOAc/hexane and 1 L of 20% EtOAc/hexane) to give three fractions. Fraction 1 was 14.0 g of two isomers (**29** and **27**): ^{13}C NMR δ 209.5, 208.5, 135.9, 135.5, 116.6, 116.4, 51.9, 49.3, 48.7, 44.1, 43.5, 41.1, 39.6, 33.2, 32.1, 31.3, 28.6, 28.4, 28.1, 25.3. Fraction

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(46) Picard, P.; Leclercq, D.; Moulines, J. *Tetrahedron Lett.* **1975**, *32*, 2731.
(47) Nakazaki, M.; Naemura, K.; Nakahara, S. *J. Org. Chem.* **1979**, *44*, 2438.

2 was 1.5 g of four isomers. Fraction 3 was 4.0 g of two isomers (**30** and **28**): ^{13}C NMR δ 209.5, 208.5, 174.1, 135.6, 116.7, 116.6, 51.8, 51.5, 50.7, 49.1, 46.2, 42.4, 41.5, 40.2, 33.9, 31.3, 28.2, 27.0, 25.6, 22.9.

Deoxygenations[31] of 2-Allylcyclohexanones. To a solution of 500 mg of fraction 1 above (2.55 mmol), 604 mg of *p*-toluenesulfonyl hydrazine (3.2 mmol, 1.25 equiv), and 64 mg of *p*-toluenesulfonic acid in 15 mL of 1:1 DMF and sulfolane at 100 °C were added 642 mg of sodium cyanoborohydride (10.2 mmol, 4 equiv) and 5 mL of cyclohexane. The mixture was heated at 100–105 °C for 1.5 h and then cooled at 25 °C. The reaction mixture was poured into 20 mL of water and extracted with three 20-mL portions of ether. The combined ethereal extract was washed with 20 mL of water, then dried ($MgSO_4$), and concentrated. The residue was chromatographed (10% EtOAc/hexane), giving 207 mg of a mixture of products (a double spot on TLC). This mixture was again chromatographed (5% EtOAc/hexane) to give 70 mg of an oil: ^{1}H NMR δ 5.75 (m, 1 H), 4.99 (m, 2 H), 3.66 (s, 3 H), 2.51 (m, 1 H, H α to CO_2Me), 2.1–1.2 (11 H); ^{13}C NMR δ 137.4, 115.4, 51.3, 40.4, 39.6, 35.5, 29.0, 26.0. Also obtained was 70 mg of another oil which was methyl *trans*-4-allylcyclohexanecarboxylate: ^{1}H NMR δ 5.75 (m, 1 H), 4.95 (m, 2 H), 3.64 (s, 3 H), 2.21 (dt, J = 3.7 and 12 Hz, 1 H, H α to CO_2Me), 2.0–0.8 (11 H); ^{13}C NMR δ 173.7, 137.0, 115.6, 51.4, 43.5, 41.5, 36.9, 31.9, 28.9.

The procedure used for the deoxygenation of fraction 1 was repeated with fraction 3. Spectral data and TLC mobilities of the two deoxygenated compounds obtained were identical with those of the products from fraction 1.

4- and 5-Carbomethoxy-2-allylcyclohexanones (18 and 27) from Cyclohexene Oxide Precursor. To a solution of 200 mg of a mixture of (1,3-dioxolanyl)-2-allylcyclohexanols (0.94 mmol) in 4 mL of THF was added 1 mL of 4 N HCl solution. After being stirred at 25 °C for 24 h, the mixture was neutralized by addition of solid $NaHCO_3$. The layers were separated. The aqueous layer was extracted with four 10-mL portions of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated to give 150 mg of a crude aldehydic oil. This oil was used in the next reaction without purification.

To a solution of 150 mg of the above aldehydes (0.89 mmol) in 10 mL of acetone at 0 °C was added dropwise a solution of Jones' reagent,[38] and the usual workup was used. The resulting oil (145 mg) was used directly in the next step without purification.

To the solution of 145 mg of the above acids in 5 mL of ether at 25 °C was added an excess of ethereal diazomethane solution.[36] The excess diazomethane was then purged by a stream of nitrogen. The solvent was removed to leave 145 mg of an oil. TLC of this oil showed two spots. Separation of these two compounds was performed chromatographically (10% EtOAc/hexane) to give 50 mg of allyl keto ester **27**: oil; ^{13}C NMR δ 209, 173.8, 135.7, 116.7, 51.8, 48.4, 42.0, 40.3, 35.0, 33.2, 29.6. The second fraction was 50 mg of 4-carbomethoxy-2-allylcyclohexanone **18**: oil; ^{13}C NMR δ 209.6, 173.7, 136.0, 116.5, 51.9, 49.4, 44.2, 43.6, 33.2, 31.4, 28.2.

The ^{13}C NMR spectral data and TLC mobility (R_f) of **27** from the two routes were identical, as were the comparisons of **18**.

Epimerization of *trans*-5-Carbomethoxy-2-allylcyclohexanone (27). To a solution of 5 mg of **27** in 1 mL of methanol was added 1 mg of sodium methoxide. The mixture was heated at reflux, and the reaction was followed by TLC. After 2 h, TLC showed the appearance of a new product which had the same R_f as **28**. This result suggested that **27** and **28** were a pair of epimers.

5-Carbomethoxy-2-allylcyclohexanols (31 and 32). To a solution of 14.0 g of a mixture of ketones **27** and **29** (71.4 mmol) in 50 mL of methanol at 0 °C was added portionwise 2.7 g of sodium borohydride (71.4 mmol, 4 equiv). After being stirred at 0 °C for 30 min, the reaction mixture was worked up in the usual manner to give 12.5 g of a crude oil. Chromatography (20% EtOAc/hexane) gave four fractions.

Fractions 1 (2.0 g) and 3 (2.5 g) were presumably the reduced products obtained from ketone **29** and were not characterized. Fraction 2 (3.0 g) was cis alcohol **32**: ^{1}H NMR δ 4.8 (m, 1 H), 4.1 (m, 2 H), 4.0 (br s, 1 H, H1), 3.65 (s, 3 H), 2.73 (m, 1 H), 2.2–1.4 (10 H); ^{13}C NMR δ 173, 136.9, 116.0, 67.6, 51.4, 40.7, 37.1, 37.0, 36.0, 28.5, 25.4. Anal. Calcd for $C_{11}H_{18}O_3$; C, 66.64; H, 9.15. Found: C, 66.50; H, 9.09. Fraction 4 was trans alcohol **31** (3.8 g): ^{1}H NMR δ 4.82 (m, 1 H), 4.1 (m, 2 H), 3.65 (s, 3 H), 3.3 (dt, 1 H, H1), 2.5–0.9 (11 H); ^{13}C NMR δ 173, 136.9, 116.3, 73.5, 51.6, 44.1, 42.0, 37.5, 36.9, 29.1, 28.2.

In an effort to confirm the structure of alcohols **31** and **32**, they were reoxidized to the starting ketone by using PCC.[24] The oxidized products from the above reactions were identical in all respects (TLC and ^{13}C NMR) with ketone **27**.

5-Carbomethoxy-2-*trans*-(3-hydroxypropyl)cyclohexanol. This compound was prepared from the *trans*-2-allylcyclohexanol **31** in 65% yield by using the same procedure previously used for the hydroboration–oxidation: ^{1}H NMR δ 3.69 (s, 3 H), 3.25 (m, 1 H), 3.05 (br s, 1 H), 2.80 (br s, 1 H), 2.31 (tt, 1 H), 2.2 (m, 1 H), 1.88–0.99 (12 H); ^{13}C NMR δ 175.4, 73.4, 62.6, 51.6, 43.8, 42.0, 37.7, 29.3, 29.2, 28.3, 28.0.

The Equatorial Epimer of 7-Carbomethoxy-*trans*-1-oxadecalin[3] (3e, A = O). The usual monotosylation procedure was used to prepare this compound starting from 430 mg of diol, giving 680 mg of the desired monotosylate which contained some tosyl chloride. The crude product was used directly without further purification.

This compound was prepared from this crude hydroxytosylate following exactly the same procedure used for the synthesis of 6-carbomethoxy-*trans*-1-oxadecalin (1, A = O): ^{1}H NMR δ 3.95 (d of m, 1 H, H2 equatorial), 3.65 (s, 3 H, equatorial CO_2CH_3), 3.41 (dt, J = 2.6 and 11.6 Hz, 1 H, H9), 2.90 (m, 1 H, H2 axial), 2.39 (tt, J = 3.7 and 12.6 Hz, 1 H, H6 axial), 2.2–1.0 (11 H) (lit.[3] δ 4.00, 3.67, 3.40, 2.93, 2.45); ^{13}C NMR δ 175.1 (CO_2Me), 80.6 (C9), 68.4 (C2), 51.4 (CO_2CH_3), 42.0 (C7), 41.3 (C10), 34.6, 30.5, 30.2, 28.3, 26.5. Anal. Calcd for $C_{11}H_{18}O_3$: C, 66.64; H, 9.15. Found: C, 66.88; H, 9.27.

Methyl 4-Allyl-3-(tosyloxy)cyclohexanecarboxylate. To a solution of 2.0 g of 5-carbomethoxy-2-*cis*-allylcyclohexanol (**32**) (10.3 mmol) in 10 mL of pyridine at 25 °C was added 3.1 g of tosyl chloride (15 mmol, 1.5 equiv). After being stirred at 25 °C for 6 days, the reaction was worked up as usual. Chromatography (10% EtOAc/hexane) gave 2.0 g of the desired tosylate (55% yield) as a white solid: ^{1}H NMR δ 7.78 (d, 2 H), 7.32 (d, 2 H), 5.55 (m, 1 H), 4.95 (m, 2 H), 4.62 (m, 1 H), 3.65 (s, 3 H), 2.41 (s, 3 H), 2.2–1.2 (10 H); ^{13}C NMR δ 175.4, 136.0, 129.7, 127.6, 127.5, 116.4, 81.6, 51.7, 39.7, 38.5, 31.2, 30.6, 24.6, 22.8, 21.5. Anal. Calcd for $C_{18}H_{24}O_5S$: C, 61.34; H, 6.86; S, 9.09; Found: C, 61.27; H, 6.86; S, 9.24.

Methyl 4-(3-Hydroxypropyl)-3-(tosyloxy)cyclohexanecarboxylate. This compound was prepared from methyl 4-allyl-3-(tosyloxy)cyclohexanecarboxylate by using the usual hydration procedure (BH_3, THF/20% NaOH/30% H_2O_2). An isolated yield of 50% of clear oil was obtained (chromatography using 50% EtOAc/hexane): ^{1}H NMR δ 7.80 (d, 2 H), 7.32 (d, 2 H), 4.85 (br s, 1 H), 3.63 (s, 3 H), 3.50 (m, 1 H), 2.60 (m, 1 H), 2.42 (s, 3 H), 2.3–1.8 (13 H); ^{13}C NMR δ 175.3, 129.7, 127.6, 80.4, 62.7, 51.6, 40.3, 37.0, 33.3, 29.7, 28.1, 25.9, 21.5. Anal. Calcd for $C_{18}H_{26}O_6S$: C, 58.36; H, 7.07; S, 8.65. Found: C, 58.20; H, 6.97; S, 8.49.

Methyl 3-Azido-4-(3-hydroxypropyl)cyclohexanecarboxylate. The procedure used previously for the preparation of azido alcohol was followed. The crude product (89% crude yield) was used directly in the next reaction: IR (neat) 3400 (br), 2100, 1730 cm^{-1}; ^{13}C NMR δ 174.6, 64.2, 62.7, 51.6, 41.9, 41.4, 33.7, 29.5, 29.3, 28.8, 27.9.

Methyl 3-Azido-4-[3-(tosyloxy)propyl]cyclohexanecarboxylate. The procedure used previously for the preparation of azido tosylate was followed. The product was isolated in 60% yield after chromatographic purification (20% EtOAc/hexane): IR (neat) 2100 (azide), 1730 cm^{-1} (ester); ^{1}H NMR δ 7.78 (d, 2 H), 7.32 (d, 2 H), 4.0 (m, 2 H), 3.68 (s, 3 H), 2.89 (m, 1 H), 2.45 (s, 3 H), 2.4–0.8 (12 H); ^{13}C NMR δ 174.4, 129.7, 127.8, 70.4, 64.1, 51.7, 41.8, 41.2, 33.7, 29.4, 28.6, 27.8, 25.9, 21.5.

The Equatorial Epimer of 7-Carbomethoxy-*trans*-1-azadecalin (3e, A = N). Starting from the above azido tosylate, this compound was prepared following exactly the same procedure used for the synthesis of **1** (A = N): IR 3350 (br, NH), 1730 cm^{-1} (CO_2Me); ^{1}H NMR δ 3.63 (s, 3 H, CO_2CH_3), 3.10 (d of m, J = 12 Hz, 1 H, H2 equatorial), 2.80 (br s, 1 H, NH), 2.64 (dt, J = 3.7 and 12 Hz, 1 H, H2 axial), 2.42–0.87 (13 H); ^{13}C NMR δ 175.1 (CO_2Me), 60.6 (C9), 51.4 (CO_2CH_3), 46.8 (C2), 42.3 (C7), 41.7 (C10), 35.0 (C8), 31.4 (C4), 31.2 (C5), 28.4 (C6), 26.1 (C3). Anal. Calcd for $C_{11}H_{19}NO_2 \cdot 0.28H_2O$: C, 65.21; H, 9.74; N, 6.92. Found: C, 65.21; H, 9.35; N, 6.59.

Cyclohexanecarboxaldehydes 33 and 34. The homologation procedure using methoxymethylenephosphorane was performed with ketone **27** obtained by oxidation of alcohol **32** (above). The resulting mixture of aldehydes obtained on hydrolysis of the enol ethers was directly subjected to equilibrating conditions with NaOMe in refluxing methanol for 2 days and then worked up as usual. Chromatography was used to separate 2.0 g of this mixture (10% ether in hexane was used as eluting solvent). Three fractions were isolated. Fraction 1 (585 mg) was assigned structure **33**: oil; ^{1}H NMR δ 9.64 (d, J = 1.6 Hz, 1 H, CHO), 4.7 (m, 1 H), 4.0 (m, 2 H), 3.66 (s, 3 H), 2.65 (m, 1 H), 2.40 (m, 1 H), 2.3–1.0 (9 H); ^{13}C NMR δ 204.3, 136.0, 116.9, 51.6, 50.2, 38.5, 37.3, 33.9, 26.5, 24.8, 24.6. Fraction 2 (514 mg) as assigned structure **34**: oil; ^{1}H NMR δ 9.59 (d, J = 3.2 Hz, 1 H, CHO), 4.7 (m, 1 H), 4.0 (m, 2 H), 3.66 (s, 3 H), 2.3 (tt, 1 H, H α to CO_2Me), 2.2–1.0 (10 H); ^{13}C NMR δ 203.6, 175.2, 135.3, 117.2, 54.0, 51.6, 41.7, 38.5, 36.2, 29.9, 28.4, 28.2. Anal. Calcd for $C_{12}H_{18}O_3$: C, 68.54; H, 8.62. Found: C, 68.29; H, 8.46. Fraction 3 (334 mg) was an oil containing some **34** and other aldehydes.

Methyl 4-Allyl-3-(hydroxymethyl)cyclohexanecarboxylates. These alcohols were prepared starting from **33** and **34** separately following the reduction procedure used before.

From **33**: 94% yield; ^{1}H NMR δ 5.75 (m, 1 H), 5.0 (m, 2 H), 3.62 (s, 3 H), 3.60 (d, 2 H), 2.62 (m, 1 H), 2.25 (m, 1 H), 2.1–1.1 (10 H); ^{13}C NMR δ 175.9, 136.9, 116.0, 64.8, 51.4, 39.8, 38.8, 37.4, 36.0, 28.6, 26.8, 25.9. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 67.79; H, 9.35.

From **34**: 87% yield; ^{1}H NMR δ 5.75 (m, 1 H), 4.98 (m, 2 H), 3.62 (s, 3 H), 3.60 (d, 2 H), 2.30 (m, 2 H), 2.1–1.2 (10 H); ^{13}C NMR δ 176.2, 136.4, 116.2, 65.0, 51.4, 43.1, 43.0, 37.5, 32.2, 31.0, 28.7. Anal. Calcd for $C_{12}H_{20}O_3$: C, 67.89; H, 9.49. Found: C, 67.79; H, 9.37.

Methyl 4-Allyl-3-[(tosyloxy)methyl]cyclohexanecarboxylates. The procedure used for the preparation of tosylates was followed to prepare these compounds, with a yield of 74.9% in the series from **33** and a yield of 74.7% in the series from **34**.

Methyl 4-(2-Hydroxyethyl)-3-[(tosyloxy)methyl]cyclohexanecarboxylates. The procedure used for reductive ozonolysis was followed to prepare these alcohols.

The series from **33**: 89.8% yield; ^{1}H NMR δ 7.76 (d, 2 H), 7.33 (d, 2 H), 4.09 (dd, 1 H), 3.97 (dd, 1 H), 3.64 (s, 3 H), 3.59 (m, 2 H), 2.56 (m, 1 H), 2.44 (s, 3 H), 2.0–1.19 (11 H); ^{13}C NMR δ 175.3, 144.7, 132.9, 129.8, 127.8, 72.1, 60.3, 51.5, 38.4, 37.5, 35.4, 32.8, 28.6, 26.8, 25.9, 21.5. Anal. Calcd for $C_{18}H_{26}O_6S$: C, 58.36; H, 7.07; S, 8.65. Found: C, 58.34; H, 6.99; S, 8.97.

The series from **34**: 80.4% yield; ^{1}H NMR δ 7.76 (d, 2 H), 7.33 (d, 2 H), 4.03 (m, 2 H), 3.64 (s, 3 H), 3.56 (m, 2 H), 2.43 (s, 3 H), 2.25 (dt, 1 H), 2.11–1.02 (11 H); ^{13}C NMR δ 175.5, 144.7, 132.9, 129.8, 127.8, 72.2, 60.1, 51.5, 42.6, 41.1, 35.9, 34.5, 32.0, 30.8, 28.4, 21.5.

The Axial and Equatorial Epimers of 7-Carbomethoxy-*trans*-2-oxadecalin (4, A = O). The procedures used for the synthesis of 6-carbomethoxy-*trans*-2-oxadecalin (**2**, A = O) were followed to prepare these compounds. The compound from aldehyde **33** was the axial epimer **4a** (A = O): oil; ^{13}C NMR δ 175.2 (CO_2Me), 72.9 (C1), 68.6 (C3), 51.5 (CO_2CH_3), 40.8 (C9), 39.0 (C10), 38.5 (C7), 33.1 (C4), 29.1 (C8), 28.8 (C5), 27.0 (C6). The compound from aldehyde **34** was the equatorial epimer[6] **4e** (A = O): oil; ^{13}C NMR δ 175.9 (CO_2Me), 72.7 (C1), 68.5 (C3), 51.4 (CO_2CH_3), 42.7 (C7), 41.4 (C9), 40.3 (C10), 33.0 (C4), 31.8 (C8), 30.2 (C5), 28.6 (C6) (lit.[6] identical).

Methyl 3-(Azidomethyl)-4-(2-hydroxyethyl)cyclohexanecarboxylate. This compound was prepared in 89% yield starting from hydroxy tosylate prepared from aldehyde **33** (above): IR 3440 (OH), 2110 cm^{-1} (N_3); ^{1}H NMR δ 3.70 (m, 2 H), 3.61 (s, 3 H), 3.37 (m, 2 H), 2.63 (m, 1 H), 2.03–1.21 (11 H); ^{13}C NMR δ 175.5, 60.5, 54.6, 51.5, 38.6, 38.1, 35.6, 34.0, 29.8, 26.9, 25.9.

Methyl 3-(Azidomethyl)-4-[2-(tosyloxy)ethyl]cyclohexanecarboxylate. This compound was prepared in 89% yield from the above azido alcohol: IR 2110 (N_3), 1740 cm^{-1} (ester); ^{1}H NMR δ 7.76 (d, 2 H), 7.33 (d, 2 H), 4.04 (m, 2 H), 3.65 (s, 3 H), 3.27 (dd, 2 H), 2.61 (m, 1 H), 2.43 (s, 3 H), 2.39–0.87 (10 H); ^{13}C NMR δ 175.1, 144.7, 133.1, 129.7, 127.8, 68.2, 54.3, 51.5, 38.4, 37.8, 33.8, 31.8, 29.7, 26.4, 25.8, 21.5.

The Axial Epimer of 7-Carbomethoxy-*trans*-2-azadecalin (4a, A = N). The procedure used for the synthesis of 6-carbomethoxy-*trans*-2-azadecalin (**2a**, A = N) was followed to prepare this compound: ^{1}H NMR δ 3.65 (s, 3 H), 3.05 (d of m, 1 H), 2.90 (d of m, 1 H); ^{13}C NMR δ 175.3 (CO_2CH_3), 52.4 (C1), 51.4 (CO_2CH_3), 46.8 (C3), 41.7 (C9), 39.2 (C7, C10), 33.5 (C4), 31.0 (C5), 29.8 (C8), 27.1 (C6). Anal. Calcd for $C_{11}H_{19}NO_2 \cdot 0.34H_2O$: C, 64.90; H, 9.75; N, 6.88; Found: C, 64.90; H, 9.31; N, 6.52.

N-Methylation of Azadecalins 1–4 (A = N). A Typical Procedure.[33] A mixture of 185 mg of amine **4a** (A = N) (0.94 mmol) and 938 mL of 37% aqueous solution of formaldehyde (11.0 mmol, 12 equiv) in 6 mL of methanol was heated at 80 °C for 1 h. The mixture was then cooled to 0 °C, and 130 mg of $NaBH_4$ (3.4 mmol, 14.5 equiv) was slowly added. After being stirred at 0 °C for 1 h, the mixture was poured into 20 mL of a saturated NH_4Cl solution. The aqueous solution was then extracted with five 15-mL portion of CH_2Cl_2. The combined organic layer was dried ($MgSO_4$) and concentrated to give 126 mg of the N-methylated product **4a** (A = NCH_3) as a white solid (84.7% yield): ^{1}H NMR δ 3.63 (s, 3 H), 2.96 (d of m, J = 11 Hz, 1 H, H equatorial), 2.82 (d of m, J = 11 Hz, 1 H, H3 equatorial), 2.68 (br s, 1 H, H7), 2.35 (s, 3 H, NCH_3), 2.19–1.96 (3 H), 1.73 (t, J = 11 Hz, 1 H), 1.56–1.09 (8 H); ^{13}C NMR δ 174.9 (CO_2Me), 61.3 (C1), 55.8 (C3), 51.5 (CO_2CH_3), 45.5, 40.4, 38.9, 37.1, 31.7, 31.1, 28.7, 27.0. Anal. Calcd for $C_{12}H_{21}NO_2 \cdot HCl \cdot 0.25H_2O$: C, 57.56; H, 8.58; N, 5.54. Found: C, 57.62; H, 8.79; N, 5.26.

1a (A = NCH_3): 75% yield; ^{1}H NMR δ 3.64 (s, 3 H), 3.12 (d of m, J = 12 Hz, 1 H), 2.62 (br s, 1 H), 2.53 (dt, 1 H), 2.47 (s, 3 H, NCH_3), 2.28–1.01 (13 H); ^{13}C NMR δ 174.2 (CO_2Me), 68.2 (C9), 56.6 (C2), 51.7 (CO_2CH_3), 39.8 (NCH_3), 38.4 (C7), 35.4 (C10), 33.3, 30.8, 26.1, 25.2, 23.0. Anal. Calcd for $C_{12}H_{21}NO_2 \cdot HCl$: C, 58.28; H, 8.96; N, 5.66. Found: C, 58.09; H, 8.77; N, 5.50.

2a (A = NCH_3): 79.9% yield; ^{1}H NMR δ 3.61 (s, 3 H), 3.01 (d of m, J = 11.6 Hz, 1 H), 2.83 (d of m, J = 11 Hz, 1 H), 2.68 (br s, 1 H), 2.34 (s, 3 H, NCH_3), 2.14 (dt, 1 H), 2.09 (br s, 1 H), 2.02 (d of m, 1 H), 1.75 (t, J = 11 Hz, 1 H), 1.54–1.14 (8 H); ^{13}C NMR δ 175.3 (CO_2Me), 61.0 (C1), 55.6 (C3), 51.4 (CO_2CH_3), 45.3, 40.2, 39.1, 36.3, 32.9, 31.4, 26.4. Anal. Calcd for $C_{12}H_{21}NO_2 \cdot HCl \cdot 0.25H_2O$: C, 57.56; H, 8.58; N, 5.54. Found: C, 57.53; H, 8.64; N, 5.37.

3e (A = NCH_3): 70.8% yield; ^{1}H NMR δ 3.58 (s, 3 H), 2.99 (d of m, 1 H), 2.35 (s, 3 H), 2.28 (m, 2 H), 1.9–0.9 (11 H); ^{13}C NMR δ 174.8 (CO_2Me), 67.8 (C9), 57.2 (C2), 51.4 (CO_2CH_3), 42.3 (NCH_3), 41.3 (C7), 39.5 (C10), 31.4, 31.3, 31.0, 27.7, 24.1. Anal. Calcd for $C_{12}H_{21}NO_2 \cdot HCl \cdot H_2O$: C, 54.64; H, 8.71; N, 5.26. Found: C, 54.99; H, 8.70; N, 4.89.

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